

Amendments to the Claims

This listing of claims will replace all prior versions, and listings of claims in the application:

1. (Original) A monoclonal antibody that specifically binds to a human VEGF with dissociation constant K_d equal to or lower than 0.2 nM.
2. (Original) The monoclonal antibody of claim 1, wherein the dissociation constant K_d is equal to or lower than 0.1 nM.
3. (Original) The monoclonal antibody of claim 1, wherein the dissociation constant K_d is equal to or lower than 0.08 nM.
4. (Original) The monoclonal antibody of claim 1, wherein the dissociation constant K_d is equal to or lower than 0.05 nM.
5. (Original) The monoclonal antibody of claim 1, wherein the dissociation constant K_d is equal to or lower than 0.01 nM.
6. (Original) The monoclonal antibody of claim 1, wherein the dissociation constant K_d is equal to or lower than 0.005 nM.
7. (Original) The monoclonal antibody of claim 1, wherein the antibody is in a form of scFv.
8. (Original) The monoclonal antibody of claim 1, wherein the antibody is in a form of Fab.
9. (Original) The monoclonal antibody of claim 1, wherein the antibody is in a form of fully assembled antibody.
10. (Original) The monoclonal antibody of claim 1, wherein the antibody is in a form of scFv and the dissociation constant K_d is measured at about 4°C, 25°C, 37°C or 42°C.

11. (Original) The monoclonal antibody of claim 1, wherein the antibody is in a form of Fab and the dissociation constant K_d is measured at about 4°C, 25°C, 37°C or 42°C.

12. (Original) The monoclonal antibody of claim 1, wherein the antibody is in a form of Fab and the dissociation constant K_d is measured at about 37°C.

13. [[14.]] (Withdrawn-currently amended) A monoclonal antibody that specifically binds to a human VEGF and has V_L comprising the amino acid sequence of

$X_1X_2X_3X_4TQX_5PSX_6X_7SX_8X_9X_{10}GX_{11}X_{12}X_{13}X_{14}IX_{15}CX_{16}X_{17}SX_{18}X_{19}IX_{20}X_{21}X_{22}X_{23}X_{24}WYQQX_{25}PGX_{26}APX_{27}X_{28}LX_{29}YX_{30}X_{31}X_{32}X_{33}LX_{34}X_{35}GVX_{36}X_{37}RFSGX_{38}X_{39}SGTDFX_{40}LTIX_{41}X_{42}LQX_{43}X_{44}DX_{45}AX_{46}YYCQQX_{47}X_{48}X_{49}X_{50}PX_{51}TFGX_{52}GTKX_{53}X_{54}IK$, wherein the underlined regions are designated as $V_L/CDR1$, $V_L/CDR2$, and $V_L/CDR3$, respectively, whereas the rest of the region is designated as framework, and wherein X_1 is D, E or A; X_2 is I, or T; X_3 is V, E, K, R, Q, or T; X_4 is M, or L; X_5 is S, or T; X_6 is S, or T; X_7 is L, or V; X_8 is A, or V; X_9 is S, or T; X_{10} is P, V, L, A, or I; X_{11} is E, or D; X_{12} is R, or T; X_{13} is A, or V I; X_{14} is T, or A; X_{15} is T, S, or A; X_{16} is S, R, N, K, H, or Q; X_{17} is A, or S; X_{18} is Q, or R; X_{19} is S, D, A, or P; X_{20} is S, G, R, T, or Y; X_{21} is T, N, S, D, or K; X_{22} is Y, or D; X_{23} is L, or I; X_{24} is A, N, or T; X_{25} is K, or I; X_{26} is Q, K, T, or I; X_{27} is R, K, Q, N, H, S, or E; X_{28} is V, or L; X_{29} is I, or V; X_{30} is F, A, G, D, or S; X_{31} is A, or T; X_{32} is S, or T; X_{33} is N, S, R, or T; X_{34} is A, H, or Q; X_{35} is S, or G; X_{36} is P, T; X_{37} is S, N, D, G, or Y; X_{38} is S, or T; X_{39} is G, or R; X_{40} is T, or A; X_{41} is S, or R; X_{42} is S, or R; X_{43} is P, or A; X_{44} is E, or D; X_{45} is F, V, or S; X_{46} is V, T, I, A, or S; X_{47} is Y, or S; X_{48} is S, Y, or N; X_{49} is S, or T; X_{50} is T, V, A, P, K, G, S, or I; X_{51} is W, or Y; X_{52} is Q, or G; X_{53} is V, or L; and X_{54} is E, D, or A.

14. [[15.]] (Withdrawn-currently amended) A monoclonal antibody that specifically binds to a human VEGF and has V_L comprising the amino acid sequence of

$X_1X_2X_3LTQPPSX_4SX_5TPGQX_6VTISCSGX_7X_8SNX_9GX_{10}NX_{11}VX_{12}WYQQX_{13}PGX_{14}APKX_{15}LX_{16}YX_{17}NX_{18}X_{19}RPSGVPX_{20}RX_{21}SGSX_{22}SX_{23}TSASLAISGLX_{24}SEDEADYYCX_{25}X_{26}WDDSLX_{27}GYVFGX_{28}GTX_{29}LTVL$, wherein the underlined regions are designated as $V_L/CDR1$, $V_L/CDR2$, and $V_L/CDR3$, respectively, whereas the rest of the region is designated as framework, and wherein X_1 is Q L, or N; X_2 is P A F, or S; X_3 is V, or M; X_4 is A, or T; X_5 is G, or A; X_6 is R, or S; X_7 is S,

or T; X₈ is S, T Y, or N; X₉ is I, or V; X₁₀ is S, or R; X₁₁ is S, P, N, A, or T; X₁₂ is N, T, or Y; X₁₃ is L, or F; X₁₄ is T, or A; X₁₅ is V, L, or F; X₁₆ is M, or I; X₁₇ is G, T, or S; X₁₈ is N, or D; X₁₉ is Q, or E; X₂₀ is D, or E; X₂₁ is F, or L; X₂₂ is K, or R; X₂₃ is G, or A; X₂₄ is Q, L, or R; X₂₅ is A, or G; X₂₆ is A, S, or T; X₂₇ is N, S, or T; X₂₈ is T, or A; and X₂₉ is K, or Q.

15. [[16.]] (Withdrawn-currently amended) A monoclonal antibody that specifically binds to a human VEGF and has V_L comprising the amino acid sequence of
QSALTQPPSVSGAPGQRVTISCTGRSSNIGAGHDVHWYQQLPGTAPKLLIYANDQRPSGVP
DRFSDSKSGTSASLGISGLRSEDEADYFCATWDDSLHGYVFGTGTKVTVL (SEQ ID No: 54).

16. [[17.]] (Withdrawn-currently amended) A monoclonal antibody is provided that specifically binds to a human VEGF and has V_H comprising the amino acid sequence of
X₁X₂QLVX₃SGGGX₄VQPGGX₅LRLX₆CAX₇SGX₈X₉X₁₀X₁₁X₁₂X₁₃GX₁₄NWX₁₅RQAPGKGX₁₆E
WVGWX₁₇NTX₁₈X₁₉GX₂₀X₂₁TYX₂₂X₂₃X₂₄FX₂₅RRX₂₆TX₂₇SX₂₈X₂₉X₃₀SKX₃₁X₃₂X₃₃YLQX₃₄NSL
RAEDTAVYYCAX₃₅YPX₃₆YYGX₃₇SHWYFDVWX₃₈QGTLVTVSS, wherein the underlined regions are designated as CDR1, CDR2, and CDR3, respectively, whereas the rest of the region is designated as framework according to Kabat nomenclature, and wherein X₁ is E, or Q; X₂ is V, or G; X₃ is Q, or E; X₄ is V, or L; X₅ is S, or T; X₆ is S T, or R; X₇ is A, or V; X₈ is Y, or F; X₉ is T, D, N, S, or A; X₁₀ is F, or L; X₁₁ is T, D, Y, A, S, or N; X₁₂ is N, H, or S; X₁₃ is Y, or F; X₁₄ is M, L, I, or V; X₁₅ is I, V, or L; X₁₆ is L, or P; X₁₇ is I, or V; X₁₈ is Y, or N; X₁₉ is T, or N; X₂₀ is E, or A; X₂₁ is P, T, or S; X₂₂ is A, or V; X₂₃ is A, H, Q, P, D, or E; X₂₄ is D, or E; X₂₅ is K, or T; X₂₆ is V, F, or L; X₂₇ is F, or I; X₂₈ is L, or R; X₂₉ is D, or N; X₃₀ is T, or N; X₃₁ is S, or N; X₃₂ is T, Q, P, or K; X₃₃ is A, V, or P; X₃₄ is L, or M; X₃₅ is K, or R; X₃₆ is H, or Y; X₃₇ is S, R, or T; and X₃₈ is G, or A.

17. [[18.]] (Withdrawn-currently amended) A monoclonal antibody is provided that specifically binds to a human VEGF and has V_L comprising the amino acid sequence selected from the group consisting of SEQ ID NOs:2-54, more preferably comprising the amino acid sequence selected from the group consisting of SEQ ID NO:14, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:44, SEQ ID NO:47, and SEQ ID NO:54.

18. [[19.]] (Withdrawn-currently amended) A monoclonal antibody that specifically binds to a human VEGF and has V_H comprising the amino acid sequence selected from the group consisting of SEQ ID NOs:57-110 and SEQ ID NOs:285-310, and preferably comprising the amino acid sequence selected from the group consisting of SEQ ID NOs:61-64, SEQ ID NO:67, 68, 70, 75, 83, 88, 89, 90, 91, 92, 93, 94, and 96-110.

19. [[20.]] (Withdrawn-currently amended) A monoclonal antibody is provided that specifically binds to a human VEGF and has CDR2 in the V_L region (V_L /CDR2) comprising the amino acid sequence selected from the group consisting of SEQ ID NOs:195-209.

20. [[21.]] (Withdrawn-currently amended) A monoclonal antibody that specifically binds to a human VEGF and has CDR3 in the V_L region (V_L /CDR3) comprising the amino acid sequence selected from the group consisting of SEQ ID NOs:210-228.

21. [[22.]]. (Withdrawn-currently amended) A monoclonal antibody that specifically binds to a human VEGF and has a framework region (FR) CDR3 in the V_L region (V_L /FR) comprising the amino acid sequence selected from the group consisting of: SEQ ID NO:229-269, and preferably comprising the amino acid sequence selected from the group consisting of SEQ ID NO:232, 235, 237, 251, 255, 263, and 265.

22. [[23.]]. (Withdrawn-currently amended) A monoclonal antibody that specifically binds to a human VEGF and has CDR1 in the V_H region (V_H /CDR1) comprising the amino acid sequence of $GX_1X_2X_3X_4X_5X_6GX_7N$, wherein X_1 is Y, or F; X_2 is D, N, T, S, or A; X_3 is F, or L; X_4 is T, D, S, Y, A, or N; X_5 is H, N, or S; X_6 is Y, or F; X_7 is M, L, I, or V.

23. [[24.]] (Withdrawn-currently amended) A monoclonal antibody that specifically binds to a human VEGF and has CDR2 in the V_H region (V_H /CDR2) comprising the amino acid sequence of $WX_1NTX_2X_3GEX_4TYX_5X_6X_7FX_8R$, wherein X_1 is I, or V; X_2 is Y, or N; X_3 is T, or N; X_4 is P, T, or S; X_5 is A, or V; X_6 is A, Q, P, H, D, or E; X_7 is D, or E; and X_8 is K, or T.

24. [[25.]] (Withdrawn-currently amended) A monoclonal antibody that specifically binds to a human VEGF and has CDR2 in the V_H region (V_H/CDR2) comprising the amino acid sequence selected from the group consisting of: SEQ ID NOs:136-156.

25. [[26.]] (Withdrawn-currently amended) A monoclonal antibody that specifically binds to a human VEGF and has CDR3 in the V_H region (V_H/CDR3) comprising the amino acid sequence of KYPX₁YYGX₂SHWYFDV, wherein X₁ is Y, or H, and X₂ is R.

26. [[27.]] (Withdrawn-currently amended) A monoclonal antibody that specifically binds to a human VEGF and has CDR3 in the V_H region (V_H/CDR3) comprising the amino acid sequence selected from the group consisting of SEQ ID NOs:311-337.

27. [[28.]] (Withdrawn-currently amended) A monoclonal antibody that specifically binds to a human VEGF and has FR in the V_H region (V_H/FR) comprising the amino acid sequence of X₁VQLVX₂SGGGX₃VQPGGX₄LRLX₅CAX₆S/CDR1/WX₇RQAPGKGLEWVG/CDR2/RX₈TX₉SX₁₀DX₁₁SKX₁₂X₁₃X₁₄YLQX₁₅NSLRAEDTAVYYCA/CDR3/WX₁₆QGTLVTVSS, wherein X₁ is E, or Q; X₂ is Q, or E; X₃ is V, or L; X₄ is S, or T; X₅ is S, T, or R; X₆ is A, or V; X₇ is I, or V; X₈ is F, or V; X₉ is F, or I; X₁₀ is L, or R; X₁₁ is T, or N; X₁₂ is S, or N; X₁₃ is T, Q, or K; X₁₄ is A, or V; X₁₅ is M, or L; and X₁₆ is G, or A.

28. [[29.]] (Currently amended) A monoclonal antibody that specifically binds to a human VEGF and has a V_L and V_H pair selected from the group consisting of: ~~SEQ ID NO:1 and 70; SEQ ID NO:1 and 67; SEQ ID NO:1 and 75; SEQ ID NO:1 and 83; SEQ ID NO:14 and 55; SEQ ID NO:1 and 101; SEQ ID NO:1 and 100; SEQ ID NO:14 and 102; SEQ ID NO:1 and 103; SEQ ID NO:1 and 104; SEQ ID NO:1 and 105; SEQ ID NO:36 and 100; SEQ ID NO:26 and 100; SEQ ID NO:28 and 100; SEQ ID NO:37 and 100; SEQ ID NO:44 and 100; SEQ ID NO:54 and 100; and SEQ ID NO:47 and 100, preferably selected from the group consisting of SEQ ID NO:28 and 61; SEQ ID NO:28 and 62; SEQ ID NO:28 and 63; SEQ ID NO:28 and 64; SEQ ID NO:28 and 68; SEQ ID NO:28 and 85; SEQ ID NO:28 and 86; SEQ ID NO:28 and 87; SEQ ID NO:28 and 88; SEQ ID NO:28 and 89; SEQ ID NO:28 and 90; SEQ ID NO:28 and 91; SEQ ID NO:28 and 92; SEQ ID NO:28 and 93; SEQ ID NO:28 and 94; SEQ ID NO:28 and 95; SEQ ID NO:28 and 96; SEQ ID~~

~~NO:28 and 97; SEQ ID NO:28 and 98; SEQ ID NO:28 and 99; SEQ ID NO:28 and 106; SEQ ID NO:28 and 107; SEQ ID NO:28 and 108; and SEQ ID NO:28 and 109; and SEQ ID NO:28 and 110.~~

29. ~~[[30.]]~~ (Withdrawn-currently amended) The monoclonal antibody of any of claims 14-29, wherein the antibody has dissociation constant K_d equal to or lower than 10 nM.

30. ~~[[31.]]~~ (Withdrawn-currently amended) The monoclonal antibody of any of claims 14-29, wherein the antibody has dissociation constant K_d equal to or lower than 1 nM.

31. ~~[[32.]]~~ (Withdrawn-currently amended) The monoclonal antibody of any of claims 14-29, wherein the antibody has dissociation constant K_d equal to or lower than 0.1 nM.

32. ~~[[33.]]~~ (Withdrawn-currently amended) The monoclonal antibody of any of claims 14-29, wherein the antibody has dissociation constant K_d equal to or lower than 0.01 nM.

33. (New) A monoclonal antibody that specifically binds to human VEGF and has a VL and VH pair selected from the group consisting of: SEQ ID NO:26 and 88; SEQ ID NO:26 and 90; SEQ ID NO:26 and 91; SEQ ID NO:26 and 106; SEQ ID NO:26 and 107; SEQ ID NO:26 and 108; SEQ ID NO:26 and 109; SEQ ID NO:28 and 88; SEQ ID NO:28 and 90; SEQ ID NO:28 and 91; SEQ ID NO:28 and 106; SEQ ID NO:28 and 107; SEQ ID NO:28 and 108; SEQ ID NO:28 and 109; SEQ ID NO:36 and 88; SEQ ID NO:36 and 90; SEQ ID NO:36 and 91; SEQ ID NO:36 and 106; SEQ ID NO:36 and 107; SEQ ID NO:36 and 108; and SEQ ID NO:36 and 109.

34. (New) A monoclonal antibody that specifically binds to human VEGF and has a VL and VH pair selected from the group consisting of: SEQ ID NO:26 and 106; SEQ ID NO:28 and 106; and SEQ ID NO:36 and 106.

35. (New) A monoclonal antibody that specifically binds to human VEGF and has a V_L and V_H pair consisting of SEQ ID NO:28 and 106.